(*c*) HOW DOES THE NEURONE DOCTRINE AFFECT THE CONCEPTION OF NERVOUS DISEASE?*

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The introduction of the neurone theory promised to bring about a general revolution in the conception of nervous disease. With a single swoop the mysteries and doubts of years were to be cleared away. Granted that the structure and function of the nervous system can be interpreted much more readily in the light of this doctrine, it still remains a question whether it has been a great assistance to us in determining the causation and development of the various diseases of the nervous system. The researches of Golgi, Ramón y Cajal, van Gehuchten, Edinger, Koelliker, Waldeyer, and the excellent work of Barker,[1] have kept us all in touch with every stage of progress in the development of the neurone theory. It was a matter of surprise to me, however, that, in spite of the interest taken in the theory, I found myself making but little reference to it in clinical lectures. The theory did not seem to add much to the teachings of former years in interpreting the various forms of brain and spinal cord disease, and other teachers of neurology, men whose opinion I value highly, have confessed to similar experiences. It is also to be noted that authors of standard works, with the possible exception of Leube and Struempell, have had little to say about the theory in its bearing upon disease, although many of them refer to the theory in an introductory chapter. With every disposition on my part to turn the new theory to fullest account, it seemed well to attempt an impartial answer to the question of the utility of this new theory in clinical teaching.

To the clinician the following points in the neurone doctrine have a special significance: It does away with the somewhat arbitrary division of cerebral, spinal and peripheral nerve disease; and a decided gain this is, for morbid processes do not always respect artificial lines; parts functionally related are apt to be simultaneously affected. It has been shown that the nervous system is composed of a series of contiguous, not continuous units; that in this nerve unit, composed of the cell-body, with its dendrites, the nerve fiber or neuraxone and the terminal tufts, the cell-body exercises an important trophic influence over the entire neurone; furthermore, that the nerve force, to speak in general terms, could travel from the cell-body to the periphery, and from the periphery to the cell-body. In the ante-neurone days the same nutritive or trophic influence over the nerve fiber was ascribed to the "cell" proper, with this difference, that we did not claim as intimate a relation between the distant nerve fiber and the ganglion cell, with which it was connected, and from which it was supposed to spring. As far as the performance of function is concerned, it matters little whether there is actual contact between terminal fibrils, or mere contiguity; the "nerve force" must in the end pass, and pass somehow from one nerve unit to the next.

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[1] The general literature of the subject may be found in Barker's work, "The Nervous System and Its Constituent Neurones," N. Y., 1899; and in the monograph by D. I. Wolfstein, of Cincinnati, "The Neurone Theory as Revealed to Brain and Nerve Diseases," Providence, 1899.

With the promulgation of the neurone theory, and the division into motor and sensory neurones the laws of Waller and of Türck were not in anywise affected, but admitted of an easier interpretation. Degeneration would set in in any part of the neurone severed from the cell-body, and in case of such severance the distal end would be the first to suffer. Goldscheider[2] is cautious enough to state that this does not preclude the possibility that a part of the neurone distant from the cell-body may take its nutrition from its immediate environment, but he thinks that such assimilation cannot be properly effected, except under the influence of the cell-body. Great as this influence of the cell-body may be over every part of the neurone, the upward degeneration which sets in after amputation of the nerve fiber proves that the health of the cell-body depends also upon the health of the distal parts. This reflection has led Marinesco[3] to develop the doctrine that if the normal function of the cell-body is to be preserved, it must receive normal peripheral stimuli. The life of the cell-body depends upon the life of its terminal parts—in other words, the cell-body and nerve fiber are interdependent; both must remain normal if the nerve unit is to perform its normal function. The case of the cell-body—to speak in legal terms—has been overstated; for the nerve fiber it has been insufficiently presented. The investigations of Ballet and Dutil, which Barker quotes, prove that changes take place in the ventral horns in polyneuritis.. It will not be amiss to present to our minds, in the case of the direct motor neurone, the great distance that intervenes between the distal end of the nerve fiber in the extremity and the cell-body in the spinal cord. We must take into account the importance to this distant part of a normal blood supply (to mention only a single condition) for the preservation of a nerve fiber, and it is evident that there are very important conditions, other than those inherent in the cell-body, upon which the health of the entire neurone must depend. We have done the peripheral fiber an injustice by making it altogether subordinate and inferior to the cell-body; it is at least co-ordinate with it in the same sense that in an electric system the wire is of no account unless the home station is in good working order; but the home station is also unable to perform its work if the wires are broken down, and they may and do break down quite as readily as the central station itself. The distal parts of the neurone—the wires—are subject to disturbances of their own. This has been shown in the case of the effect of the various toxic agents, for these seem to exert their influence chiefly upon the distal parts of the neurone, and possibly in secondary fashion only upon the cell-body. The farther away from the cell-body the diseased fiber lies, the greater the damage; possibly, also, the greater the difficulty of repair. It would be a natural and logical consequence to expect alterations in the cell-body whenever the peripheral parts of the neurone is affected by disease, by poisoning, or by injuries of any sort. It may be claimed that former methods were insufficient to prove that such changes actually occurred in the ganglion cell, and that it will require careful examination by the most recent staining methods to prove or disprove the intimate relation between the fiber and the home station. To uphold the full dignity of the cell-body and to account for the fact that its structure, as far as at present made out, does not seem altered for a long period of time after the distal parts have been affected, Erb and others have formulated the theory that the cell may be altered in function, and thus exert a perverse and insufficient influence over the distal parts, without exhibiting any great change in its structure. To such straits are we put in upholding the paramount influence of the cell proper. Attractive as this theory is, there is danger lurking in it, for we are piling theory upon theory, without having sufficient evidence, or without even the hope of being able to give substantial proof of the correctness of this additional doctrine. It will surely be safer, in view of all these perplexing theories and explanations, to hold to the statement that the cell-body and nerve fiber are functionally co-ordinate and equally important parts of the entire neurone system.

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[2] Berliner klin. Wochen schr. 1894, Nos. 19 and 20.

[3] Neurolog. Centralblatt 1892. P. 463 *et seq.*

This question of the trophic influence of the cell-body had to be discussed before we could attempt to appreciate the value of the neurone in its relation to disease of the nervous system. The doctrine helps us, of course, very little in our understanding of the acute and inflammatory processes, for such processes do not respect the finer structure of the brain or cord, and are generally so destructive that it would matter little whether the nervous system were made up of contiguous or continuous units. Allusion was made above to toxic diseases, and the neurone doctrine has been of the greatest possible assistance in reconciling the different findings that have been reported by various authors in regard to the effect of poisons upon the peripheral nerves and the spinal cord. It was difficult in former days to account for the claim put forth by many that in lead poisoning the peripheral nerves were diseased, while the experiments upon animals by Stieglitz and the post-mortem findings in the human body showed that in extreme cases, or at least in some instances, the cells of the spinal cord were affected as well. It simplifies matters very much to be able to claim that lead and other poisons exert their chief influence over the direct motor neurone, and that it matters little whether in a given case the central or distal part of the neurone may be involved. The doctrine also helps us to account for the occurrence of polyneuritis and poliomyelitis in those rare cases that have been reported by Gowers, and we must suppose that organic as well as inorganic poisonous products may affect the various parts of the peripheral neurone; in the interpretation of such conditions the doctrine has been distinctly helpful.

Much has been claimed for the aid which the neurone doctrine offers in the interpretation of the degenerative diseases of the central nervous system, whether such degeneration affect primarily the gray or the white matter. Tabes dorsalis is to be accepted as a disease of the direct sensory neurone; whatever the nature of the poison circulating in the body may be, the sensory fiber is the part primarily affected. Even if the view could be maintained that the disease began in the spinal ganglion cell, this ganglion cell would not be diseased unless there was something wrong about the peripheral stimuli conveyed to it. But is there any evidence that the disease does actually begin in the most distal parts of the neurone? Wolfstein, who has written an excellent summary of the entire question, refers to the fact that Batten has shown that in tabes the muscle spindle presents the distinct evidence of disease. We have here a peripheral organ of sense, as this author says, which transmits external impressions to the peripheral sensory fiber, which is seen to undergo degeneration. "Armed with the hypothesis of Bechterew of the vital influence of the sensory end apparatus upon the character of the afferent impressions and with the theory of Marinesco regarding the necessity for the continuance of the function, in order that the nutrition and the power of the trophic center be maintained, we can readily understand the changes which follow the degeneration of the sensory ending." Plausible as this explanation is, it must be claimed that such muscle spindle changes have not been established in a sufficient number of cases to warrant us to utilize them in the attempt to explain the origin of the morbid changes of tabes; and, without being facetious, we might supplement Wolfstein's remarks by saying that if we are armed with hypotheses enough, we can explain almost anything and everything. If Fraenkel is right in maintaining that even the motor palsies of tabes are dependent upon changes in the deep sensibility, such palsies would not militate against the neurone theory of the disease, and possibly Batten's findings may also explain the occasional occurrence of marked muscular atrophies in tabes. After all has been said that can be said in favor of this newer doctrine, we now speak of tabes as a disease of the direct sensory neurone, whereas in former days, we considered it a disease primarily affecting the sensory nerve systems. In view of the probable and frequent syphilitic origin of the disease, it is of course helpful to know that the products of syphilitic poisoning affect chiefly the direct sensory neurone; other poisons having a predilection for the motor neurones.

A consideration of the neurone doctrine has also led to a better understanding of the spinal form of progressive muscular atrophy, and of its relation to progressive bulbar palsy and to amyotrophic lateral sclerosis. The first two forms evidently represent primary degenerations of the direct motor neurone, either in the spinal cord or in the lower portion of the brain axis. Of course, we are still at a loss to know why such degeneration should set in in the few individuals affected by the disease, but we accept such degeneration as a fact. Amyotrophic lateral sclerosis would in the light of this theory represent the same primary degeneration affecting the cortical cells of the indirect motor neurone, as well as the direct motor neurone; or, as Kahler and Moebius put it, amyotrophic lateral sclerosis represents a primary degeneration of the various portions of the cortico-muscular tract. But in this disease in the direct motor neurone the cell-body is the part primarily affected; in the indirect motor neurone the distal part is the part first diseased, and the attempt to show that these distal parts are dependent upon functional, if not structural, changes in the far-distant pyramidal cell-body has not been entirely satisfactory. To be sure, such changes have possibly not been established because the necessary investigations have not yet been made. But here again it will not do to pile theory upon theory, until concrete findings shall have been reported which tend to uphold this view. It is not an unnatural thought to suppose that in a form of cord disease of one neurone, it may in some instances spread to the distal part of a neighboring neurone, and it seems much more plausible to think of the morbid influence exerted by a degenerated or degenerating neurone upon neighboring fibers than to suppose that such degeneration in the direct motor neurone is due to problematic affections of the distant pyramidal cell. I shall be inclined to the opinion that even if, in some instances, changes in the pyramidal cells were found, that these would be entirely secondary to the changes in the distal parts.

It would be natural also to expect further light from this doctrine upon the relation of the various forms of progressive muscular atrophy to the Aran-Duchenne type. It is surprising to know that no author has as yet referred to the controversial findings in the case of the peroneal form of progressive muscular atrophy. Hoffmann, as is well-known, maintains that it is due to a progressive neuritis—in other words, that it is neural in origin; whereas, equally reliable investigators have shown that in some instances the spinal cord has been involved. It is always difficult to ascertain whether such involvement is primary or secondary; but the conflicting views can be reconciled if we regard this form of progressive muscular atrophy as a degeneration of the direct motor neurone; the degeneration in some instances affecting the distal parts and in some the central part of the neurone. Some doubt has of late been cast upon the radical differences which were supposed to exist between the amyotrophies and the progressive muscular dystrophies. It is possible, if not probable, that the muscular fiber is subject to primary degeneration, without any reference to the terminal nerve plate, but it would be a grateful task to examine the peripheral nerve endings in the earlier stages of the progressive dystrophies, to determine whether or not these are altered. Such changes as I found in the peripheral nerve in a typical progressive muscular dystrophy might well be secondary to a primary degeneration of the muscle, for any marked change in the muscular tissue by removing the normal peripheral stimulus should in the course of time affect the peripheral nerve endings. On this special point I am in hopes of shedding some light by an examination of a case of progressive muscular dystrophy now under investigation. The neurone doctrine, if it does not clear up a number of the questions still under dispute regarding muscular dystrophies, will at least give additional interest to the investigation of these diseases, which seemed only a short time ago to have been thoroughly studied and almost exhausted.

The combined scleroses of the cord which have been so difficult to explain may also admit of somewhat readier interpretation, if we choose to accept the view at which I hinted that the disease of one neurone may affect the neighboring distal parts of another neurone. The older conception of the systemic diseases of the central nervous system will, no doubt, have to yield to the more modern doctrine that disease affects parts functionally if not structurally related. It will also tend gradually to minimize the importance of the older anatomical divisions of nervous disease into diseases of the brain, of the spinal cord and of the peripheral nerves, and no doubt the general interpretation of disease will be materially helped if we substitute, as far as possible, physiological for the older and anatomical sub-divisions. It is not necessary to enter upon a discussion of the aid rendered by the neurone doctrine in the interpretation of mental diseases. The attempt has been made to apply the doctrine to the elucidation of general paresis. To say that the associative, motor, and sensory nerves are involved is to hold that every part of the central nervous system is more or less diseased; it would be of some interest, and would bring out in the strongest light the relation of general paresis to tabes, if it could some day be shown that in general paresis also, the sensory neurones are primarily affected. It is altogether premature to attempt an explanation of other forms of mental derangement in the light of the new theory. I cannot sympathize with a recent author (Wolfstein) who believes that the neurone doctrine "has reconciled the physical and the metaphysical, it has bridged over the chasm between the material physiologist and the metaphysical physiologist, and joined their hands in harmony."

Nor can I find sufficient reason for the present to apply the neurone doctrine to the interpretation of functional diseases and functional conditions. To speak of irritable sensory neurones is just about as vague as to refer to spinal irritability, as we did in former days. A substitution of words does not imply an increase in our own concepts. The defense of the retraction theory I must leave to one of its chief apostles, who is fortunately in our midst.

Let me conclude by saying that the neurone theory is of distinct assistance in the interpretation of toxic diseases, affecting at one and the same time the peripheral and central nervous systems, while in some instances involving only one or the other, and not both parts; it has shed some light upon the perplexing questions of the relations of the various forms of progressive muscular atrophy, and upon the early morbid changes in tabes. It may be of some further help in our understanding of the combined scleroses. More than this can scarcely be claimed for it; if it shall have accomplished all of this, and shall be able to stand the test of further sane criticism, it will be entitled to the consideration it has already received.

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100 UN CAS DE TORTICOLLIS MENTALE (A Case of Mental Torticollis. E. Nouges et J. Sirol (Nouvelle Icon. de la Salpêtrière, Nov. et Dec., 1899).

Brissaud first called attention to this form of spasmodic tic. The condition is not very rare; the case is as follows: A gardener, thirty years old. Father and grandfather had stuttering speech. The patient began to stammer at the age of eight years; this condition increased in intensity up to twenty years, when it diminished somewhat, manifesting itself only at times of emotional excitement. In the month of September, 1898, without any apparent cause he felt his head drawn to the right side; shortly after this, to the left side. On attempting to restrain this movement, a spasmodic contraction of the sterno-cleido-mastoid muscle was produced; after a few contractions, the head was in its normal position. These movements increased in variety and frequency, the trapezoid muscle taking part in them. He learned to stop them after a time by pressure of the fingers on the opposite side of the chin, nose, etc. There is no doubt that the condition in this case was exclusively psychical. Bempaire has said that in all cases of mental torticollis, evidences of degeneracy are to be found. In this case there was present hereditary condition of stuttering, which points in the same direction. The author concludes that mental torticollis is a spasmodic tic, and all tics of a mental origin develop often, if not always, in degenerates. SCHWAB.